

Office Action Summary	Application No. 10/523,802	Applicant(s) LOCHER ET AL.	
	Examiner Kristie L. Brooks	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-13,16 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-13,16 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application

1. Claims 1, 5-13 and 16-17 are pending.
2. Receipt and consideration of Applicants remarks and English translation of certified priority document filed on December 28, 2007 is acknowledged.
3. Due to Applicant submission of a certified English translation of Applicants priority document, the Final Rejection mailed on October 4, 2007 is vacated and new grounds of rejections are presented below.

Withdrawn Rejections/Objections

4. The objection to the disclosure for the use of trademarks is withdrawn in view of Applicant amendments filed on July 16, 2007
5. The rejection of claims 14-15 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicant amendments filed on July 16, 2007
6. The rejection of claims 1-4,6-8, and 10-15 under 35 U.S.C. 102(e) as being anticipated by Barsig (US Pub No. 2003/00992706) is withdrawn in view of Applicant amendments filed on July 16, 2007.
7. The rejection of claims 1, 3, 5-6, 8 and 9 under 35 USC § 102(b) as being anticipated by Keller et al. is withdrawn in view of Applicant amendments filed on July 16, 2007.

New Grounds of Rejections

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claim 1, 5-13 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barsig (US Pub No. 2003/00992706) in view of Buris et al. (Loteprednol etabonate, a new soft steroid is effective in a rabbit acute experimental model for arthritis, *Pharmazie*, Jan;54(1):58-61,1999).

Applicant claims a composition comprising loteprednol or pharmaceutically acceptable ester thereof and N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide.

Determination of the scope and content of the prior art**(MPEP 2141.01)**

Barsig teaches the combined administration of a PDE4 or PDE3/4 inhibitors, such as N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide, also known as AWD-12-281, and disease modifying anti-rheumatic drugs (DMARDs) such as budesonide, mometasone furoate, etc., for the treatment of diseases such as rheumatoid arthritis or allergic rhinitis/sinusitis (see the abstract, page 1 paragraphs 1,17-18; page 2 paragraphs 19-22; page 3 paragraphs 30-32; page 4 paragraph 33; page 6 paragraphs 50-51). The combination is said to delay the onset and reduce the symptoms of rheumatoid arthritis (see page 1, paragraph 15). The expression "disease modifying anti-rheumatic drugs (DMARDs) are those compounds which are useful in the treatment of rheumatoid arthritis (see page 3 paragraph 32). The medicaments containing the PDE inhibitor and the DMARD, either alone or in a fixed combination, are employed in the form of tablets, capsules, patches, suppositories, suspensions or solutions either together or separately, and can be formulated with various excipients or vehicles suitable for desired pharmaceutical formulations (see page 6 paragraphs 50-53; page 7 paragraph 54). The combined use (i.e. simultaneous, sequential or separate administration) of PDE4 or PDE3/4 inhibitor and a DMARD may also include a medicament pack containing both the PDE4 or PDE3/4 inhibitor and a DMARD as discrete separate dosage forms and instructions for the simultaneous, sequential or

Art Unit: 1616

separate administration of both discrete separate dosage forms (see the entire article, especially paragraphs 17-20 and claims 1-6).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Barsig does not teach the use of loteprednol etabonate in combination with a PDE4 or PDE3/4 inhibitor. This deficiency is cured by the teachings of Buris et al.

Buris et al. teach loteprednol etabonate, a new soft steroid designed for use as a local therapeutic, in a rabbit experimental model for arthritis. Co-administration of either dexamethasone or loteprednol etabonate directly into the joint effectively blocks the inflammatory response. The steroid treatments prevented the adverse inflammatory effects of antigen action. These results indicate that loteprednol etabonate is a much safer drug and could provide a therapeutic advantage over currently used intra-articular steroids for alleviating rheumatoid arthritis (see the abstract).

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use loteprednol etabonate in the instant composition.

Art Unit: 1616

One of ordinary skill in the art would have been motivated to do this because the combination of N-(3,5-dicholopyridin-4-yl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide and disease modifying anti-rheumatic drugs (DMARDs) (i.e. drugs useful in the treatment of rheumatoid arthritis) is already known in the art as suggested by Barsig. Although Barsig does specifically teach the use of loteprednol etabonate, it would have been obvious to one of ordinary skill in the art to employ loteprednol etabonate because loteprednol etabonate is also a DMARD (as defined by Barsig) that has a therapeutic advantage over current steroids used in the treatment of rheumatoid arthritis. Thus, one of ordinary skill in the art would have been motivated to substitute loteprednol etabonate into the formulations taught by Barsig if one wanted to use a safer drug and also enhance the therapeutic benefit of the combination taught by Barsig in the treatment of rheumatoid arthritis. Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed composition.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kristie L. Brooks whose telephone number is (571) 272-9072. The examiner can normally be reached on M-F 8:30am-6:00pm Est..

Art Unit: 1616

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KB

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616